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10/589,717	08/16/2006	Bo-Lennart Johansson	PU0460	8795

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GE HEALTHCARE BIO-SCIENCES CORP.
PATENT DEPARTMENT
800 CENTENNIAL AVENUE
PISCATAWAY, NJ 08855

EXAMINER	
SAUNDERS, DAVID A	
ART UNIT	PAPER NUMBER
1644	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/589,717	JOHANSSON ET AL.	
	Examiner	Art Unit	
	David A. Saunders	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/16/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

AMENDMENT ENTRY

Amendment of 8/16/06 has been entered. Claims 1-30 are pending and are under examination.

OBJECTION(S) TO CLAIMS

Claims 5, 18 and 19 are objected to under 37 CFR 1.75(i), as being of improper form for failing to indent each active verb step or component.

In claims 5 and 18, there are 3 active verb steps of "contacting", "adding" and "contacting". None of these are indented.

In claim 19, there are 3 kit components recited as "a first chromatography column", "a second chromatography column" and "one or more buffers". None of these are indented.

Claim 4 is objected to because of the following informalities: At line 2 "one or further" is believed intended to be –one or more further--. Appropriate correction is required.

REJECTION(S) UNDER 35 USC 112, SECOND PARAGRAPH

Claims 1-5, 7, 9-12, 17, 20 and 25-30 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claims 1, 7, 17, 20, 25 and 30, it is not clear what "selected from the group consisting of carbon (C), sulfur (S) and oxygen (O)" is referring to. An "aromatic or heteroaromatic entity" inherently contains "C"; thus, why is applicant bothering to list "C" after "selected from"? Any "aromatic" ring system would only contain "C"; thus why is applicant further defining the "aromatic" ring system by reciting that the ring atoms are "selected from the group consisting of C, S or O"? Because of this rejection, claims 2-4 and 26-29, that depend from claim 1, are included in the list of rejected claims.

In claims 9 and 11-12, "the second chromatography step" lacks antecedent basis In base claim 5 there is a "second chromatography column", but the step that recites this is recited as a "contacting" step, rather than a "chromatography" step.

In claim 17, line 3 "the ligands" lack antecedent basis.

DOUBLE PATENTING CONSIDERATIONS

The instantly pending claims have been compared to the claims of copending application 10/589,718 (see US 2007/0112178, cited on PTO-892). The claims of copending application 10/589,718 have been amended since this publication was printed. Because of the amendment, the instant claims are not rejected under obviousness type double patenting over the claims of copending application 10/589,718.

REJECTION(S) UNDER 35 USC 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-4, 17 and 23-30 are rejected under 35 U.S.C. 102(b) as being anticipated by Lihme et al (6,498,236), cited on 1449).

Lihme et al teach a chromatography resin having a multi-modal ligand, which comprises a mono- or bicyclic aromatic or heteroaromatic ligand and an acidic

substituent, such as a carboxylic acid. See abstract; see col. 5, lines 25-67; col. 15, lines 25-41. The carboxylic acid substituent would serve as a weak cation exchanger, in accord with instant dependent claim 27, in view of the fact that applicant's own disclosure teaches that a carboxylic acid group can serve as a weak cation exchanger. Though Lihme et al do not verbatim teach that the carboxylic group serves as a weak cation exchanger, such is what the carboxylic acid group inherently is. The nature of the mono- or bicyclic aromatic or hetero aromatic ligand is disclosed at col. 13, line 19-col. 14, line 67. Numerous of these have structures consistent with the concluding limitations of instant claims 1 and 17, as well as with the limitations of dependent claims 2-3. As such, the affinity ligands of Lihme et al are multi-modal".

Lihme et al teach the contacting step of instant claim 1. See the abstract; see, for example, col. 5, lines 54-60; col. 6, lines 35-52. The contacting step adsorbs immunoglobulin/ antibody to the resin. Some contaminants wash through the column, while other contaminants adsorb to the column. Adsorbed immunoglobulin/antibody and contaminants are then differentially eluted from the resin, See, for example, col. 6, line 54-col. 7, line 57. The immunoglobulin/antibody being purified can be from a variety of sources; see col. 8, lines 7-24; col. 9, line 18- col. 10, line 32.

Regarding claim 4, Lihme et al teach further purification steps (e.g. col. 7, lines 37-47).

Regarding claims 26 and 28, Lihme et al teach purification of monoclonal antibodies from hybridoma cell cultures (e.g. col. 1, lines 30-34; col. 9, lines 18-26).

Regarding claim 29, Lihme et al teach purification of immunoglobulins from sources such as animal plasma or sera, or colostrum (e.g. abstract). Any of these sources of immunoglobulins would contain polyclonal antibodies.

From the above, method claims 1-4 and 26-29 are anticipated.

Regarding claims 23-25 and 30, drawn to a disposable column with a multimodal ligand, Lihme et al show chromatography columns. Though Lihme et al point to the regeneration, and hence reuse thereof (e.g. col. 6, line12; col. 8, line 6), they also indicate that regeneration is not mandatory (col. 6, lines 14-20). In any case, whether the column is regenerated or not, any column can be thrown out and is hence

disposable. Since applicant has not defined what materials would be used to manufacture a disposable, as opposed to a non-disposable column, anticipation is stated.

Numerous portions of applicant's disclosure have pointed to distinctions between the instant invention and Pat. 6,498,236 of Lihme et al. However, these distinctions pertain to features which are not recited in the instant claim limitations.

Claims 1-10, 16-18, 23-27 and 29-30 are rejected under 35 USC 102(b) or (e) as anticipated by Belew et al (US 6,852,230 or WO 02/053288, cited on 892).

WO 02/053288 has 102(b) date, as of its publication date of 7/11/02, since it was published more than one year prior to applicant's Swedish priority date of 2//27/04. US 6,852,230 has a 102(e) date of 6/19/03. For convenience the examiner will only refer to US 6,852,230 by col. and line numbers. No copy of WO 02/053288 is presently provided to applicant; an imaged copy of this reference may be found in the file record of copending Ser. No. 10/589,718

Belew et al teach multi-modal affinity ligands containing an aromatic or heteroaromatic ring and a carboxylic acid group, as a weak cation exchange group. Proteins such as BSA or IgG can be adsorbed thereto and then eluted therefrom. See the ligands listed in Table I, with the absorbance maximum and recovery percentages indicated. From the structures of the mono- or bicyclic aromatic or hetero aromatic ligands disclosed in Table I, it is noted that numerous of these have structures consistent with the concluding limitations of instant claims 1 and 17, as well as with the limitations of dependent claims 2-3. Thus instant claims 1-3 and 17 are anticipated.

With respect to dependent claim 4, note the teaching that there can be further purification steps, such as "traditional ion-exchange chromatography (col. 1, line 66-col. 2, line 12 and col. 3, lines 10-27).

With respect to independent claims 5 and 18, as well as dependent claims 9-10, all steps are shown by the teaching of further purification steps, such as "traditional ion-exchange chromatography (col. 1, line 66-col. 2, line 12 and col. 3, lines 10-27).

For dependent claims 6 and 26, note cell cultures taught at col. 13, lines 42+.

Regarding dependent claims 8 and 27, the taught carboxylic acid group is a weak cation exchange group.

Regarding dependent claims 16 and 29, the exemplified IgG preparations would contain polyclonal antibodies.

From the above noted teachings, instant method claims 1-10, 16-18, 23-27 and 29-30 are anticipated.

Regarding claims 23-25 and 30, drawn to a disposable column with a multimodal ligand, Belew al show chromatography columns. Though Belew et al do not particularly mention "disposable columns", any column can be thrown out and is hence disposable. Since applicant has not defined what materials would be used to manufacture a disposable, as opposed to a non-disposable column, anticipation is stated.

Claims 1-3, 23-25, 27 and 29-30 are rejected under 35 U.S.C. 102(a) as anticipated by Johansson et al (Jour. Chromat. A, 1016, 35, 2003, cited on 1449).

Johansson et al teach multi-modal affinity ligands containing an aromatic or heteroaromatic ring and a carboxylic acid group, as a weak cation exchange group. Proteins such as BSA, human IgG, or lysozyme can be adsorbed thereto and then eluted therefrom. Johansson et al teach that such multi-modal affinity ligands can be used in purification processes (pages 36 and 48).

Regarding the concluding limitations of instant claim 1, as well as the limits of dependent claims 2-3, the structures shown by Johansson et al for ligands 2, 4, 5, 8, for ligands 3, 6, 10, for ligand 7, for ligands 11, 17, and for ligand 15 (see Fig. 3) have ring atoms that meet these limitations.

As such, instant method claims 1-3 and 27 are anticipated.

Regarding dependent claim 29, the IgG exemplified would have polyclonal antibodies.

Regarding claims 23-25 and 30, drawn to a disposable column with a multimodal ligand, Johansson al show chromatography columns. Though Johansson et al do not particularly mention "disposable columns", any column can be thrown out and is hence disposable. Since applicant has not defined what materials would be used to

manufacture a disposable, as opposed to a non-disposable column, anticipation is stated.

Claims 1-3, 23-25, 27 and 29-30 are rejected under 35 U.S.C. 102(a) or (e) as anticipated by Maloisel et al (WO 03/024588, cited on Form 1449).

WO 03/024588 has 102(a) date, as of its publication date, since it was published within one year prior to applicant's Swedish priority date of 2//27/04. WO 03/024588 has a 102(e) date, as of its filing date, since it is published in English and designates the US.

Maloisel et al (WO 03/024588) teach mixed-mode/multimodal affinity ligands for cation exchange chromatography. Numerous of the ligands shown in Tables 1A (pp 35-36) and 1B (p 40) and Table 2 (p 44) have an aromatic or heteroaromatic ring and a carboxyl group, as a weak cation exchange group. Numerous of these aromatic or heteroaromatic rings have a structure consistent with the concluding limitations of instant claim 1, as well as the limits of dependent claims 2-3. Maloisel et al teach that such multi-modal affinity ligands can be used in purification processes (pages 20-23). Proteins such as Cyt-C, BSA, human IgG, or lysozyme can be adsorbed thereto (Examples 12-14). Hence the method of instant claims 1-3 and 27 is anticipated.

Regarding dependent claim 29, the IgG exemplified would have polyclonal antibodies.

Regarding claims 23-25 and 30, drawn to a disposable column with a multimodal ligand, Maloisel et al show chromatography columns. Though Maloisel et al do not particularly mention "disposable columns", any column can be thrown out and is hence disposable. Since applicant has not defined what materials would be used to manufacture a disposable, as opposed to a non-disposable column, anticipation is stated.

REJECTION(S) UNDER 35 USC 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 5, 11, 13-15 and 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Belew et al in view of Priorl et al (5,118,796, cited on Form 892).

The Belew et al reference has been cited supra, against claim 5, for showing a method involving the contacting of antibodies/immunoglobulins with a multi-modal chromatography medium/ matrix/resin, followed by the addition of an eluent to release the antibodies/immunoglobulins therefrom. The eluate is then further purified via a second chromatography step, such as an ion-exchange chromatography step. Prior et al show a similar sequence of steps in method involving the contacting of antibodies/immunoglobulins with a cation chromatography medium/ matrix/resin, followed by the addition of an eluent to release the antibodies/immunoglobulins therefrom. The eluate is then further purified via a second chromatography step, which is an anion-exchange chromatography step. Since the sequences of steps taught by both Belew et al and Prior et al are similar, it would have been obvious that the second chromatography step of Belew et al would be conducted with an anion exchange resin. Thus instant dependent claim 11 would have been obvious.

Regarding dependent claims 13-14, note Fig. 1 of Prior et al. This teaches an embodiment in which the immunoglobulin is adsorbed to and then eluted from the anion exchange column (right most track of Fig. 1) and an embodiment in which the immunoglobulin flows through the anion exchange column (middle track of Fig. 1).

Regarding dependent claim 15, Prior et al show purification of monoclonal antibodies (col. 9, lines 10+).

The Belew et al reference has been cited supra, against claim 1 for showing a method involving the contacting of antibodies/immunoglobulins with a multi-modal chromatography medium/ matrix/resin, such that the antibodies are adsorbed thereto; regarding dependent claim 28, Prior et al show purification of monoclonal antibodies (col. 9, lines 10+).

Claims 19-20 and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Belew et al in view of Hunt et al (US 2002/0110495, cited on Form 892).

The Belew et al reference has been cited supra, against claim 5, for showing a method involving the contacting of antibodies/immunoglobulins with a multi-modal chromatography medium/ matrix/resin, followed by the addition of an eluent to release the antibodies/immunoglobulins therefrom. The eluate is then further purified via a second chromatography step, such as an ion-exchange chromatography step. Hunt et al show that it was known to provide one or more chromatography media/ matricies/ resins, in a kit, along with buffers. The chromatography media/ matrices/ resins provided in the kit can be of a variety of types, including ion exchange resins.

Since the primary reference shows chromatography media/matrices/resins and various buffers (e.g. equilibration, loading, elution, and/or regeneration buffers), provision of these in a kit form, as in claim 19, would have been obvious. It has been stated supra that the primary reference shows a chromatography medium/matrix/resin that has a structure consistent with the limits of claim 20; therefore claim 20 would have been obvious.

In this rejection, no weight is given to the instructions. Instructions are merely printed matter and cannot distinguish over the prior art. In re Nagai 70 USPQ2 1862.

Regarding claim 22, drawn to the embodiment in which the first column is a disposable column, Hunt et al teach disposable/discardable columns, in the form of plastic pipette tips. See para. [0040].

Claims 23-25 and 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over any of Lihme et al, Belew et al, Johansson et al or Maloisel et al in view of Hunt et al (US 2002/0110495, cited on Form 892).

Each of the primary references has bee cited supra as anticipating the multimodal columns of instant claims 23-25 and 30. Anticipation was stated on the basis that any column can be a "disposable column", in the sense that it can be thrown out and is hence disposable. In the event that applicant thinks that more weight should be given to the recitation of "disposable", the office shall rely upon Hunt et al for teaching disposable/discardable columns, in the form of plastic pipette tips. See para. [0040].

Claim 21 is rejected under 35 U.S.C. 103(a) as being unpatentable over Belew et al in view of Hunt et al, as applied to claim 19 above, and further in view of Welt et al (US 2002/0187144, cited on Form 892).

Welt et al show the further feature that, when one is conducting multiple chromatography steps in the preparation of an antibody for therapeutic use, it is desirable to use sterile columns. See para. [0034] and [0036]. Thus it would have been obvious to have provided the ion exchange columns, taught by Belew et al, as sterilized columns in a kit.

IDS REFERENCES NOT CONSIDERED

The WO 02/59059 reference has been lined through on attached form 1449, since it has nothing whatever to do with chromatography. It is believed that applicant intended to, instead, submit WO 02/05959.

ART OF INTEREST

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Cooper, Jr, Bodor et al, and Nelson et al (all cited on PTO-892) show that disposable ion exchange columns/cartridges were well known in the art. Mukhamedyarov et al (cited on PTO-892) show sterile ion-exchange columns.

CONTACTS

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David A. Saunders, whose telephone number is 571-272-0849. The examiner can normally be reached on Mon.-Thu. from 8:00 am to 5:30 pm and on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Eileen O'Hara, can be reached on 571-272-0878. The fax phone number for the organization where this application is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Typed 3/12/08 DAS

/David A Saunders/

Primary Examiner, Art Unit 1644